claims 150-157 are added. After entry of this amendment claims 32-34, 36-43, 77, 79-86, 112-116, 118-120, 122, 124, 126, 128, 130, 132-136, 138-140, 142, 144, 146, 148 and 150-157 will be pending.

OBJECTIONS TO THE SPECIFICATION

The Examiner has objected to the specification for containing an embedded hyperlink and/or other form of browser-executable code. Applicant has amended the specification so that the URLs located at pages 8 and 14 will not form a hyperlink when the patent based upon this application is issued. As such, Applicants request that the objection to the specification be withdrawn.

CLAIM REJECTIONS - 35 U.S.C. §112

The Examiner has rejected claims 32-43, 77-86 and 112-149 under 35 U.S.C §112, first paragraph as allegedly containing subject matter which was not described in specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention.

The Examiner states that the prior art provides only 3 nucleic acid sequences encoding monocot thioredoxins: 2 wheat thioredoxins and one rice thioredoxin in addition to the barley thioredoxin sequence disclosed in the present application.

Applicants respectfully disagree with the Examiner's grounds for rejection and the above statement. However, in order to facilitate prosecution in this case applicants have amended the pending claims, without prejudice or disclaimer, to recite nucleic acids encoding barley, rice, *Arabidopsis*, soybean, wheat, tobacco, and Brassica thioredoxin polypeptides for the pending claims. The specification at page 3, lines 5-17 supports each claimed species of thioredoxin. In contrast to the Examiner's assertion, nucleic acids encoding the barley, rice, *Arabidopsis*, soybean, wheat, tobacco and Brassica thioredoxin polypeptides are known in the prior art and are readily available to one of

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ordinary skill in the art. For example, Rivera-Madrid *et al.*, PNAS **92**, 5620-5624 (1995) (cited as Paper No. 9, Form PTO-892, Nonpatent Document V) discloses five divergent thioredoxin sequences in *Arabidopsis*. Shi *et al.*, Plant Mol. Bio. **32**: 653-662 (1996) discloses a series of soybean thioredoxin sequences. References supporting tobacco and Brassica thioredoxin are further provided in the specification at page 3, lines 7-8.

Applicants reserve their right to pursue claims to the canceled subject matter in one or more continuation applications.

Applicants assert that the pending claims meet the requirements of 35 U.S.C. §112, first paragraph. Applicants respectfully reserves the rights to pursue claims to the canceled subject matter in one or more continuation or divisional cases.

CLAIM REJECTIONS - 35 U.S.C. §103

A. The Examiner's Rejections

The Examiner has rejected claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 78, 82, 83, 84, 85, 112, 113, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 133, 134, 136, 138, 140, 142, 144, 146 and 148 under 35 U.S.C. §103(a) as being unpatentable over Rodriguez (US 5,889,189) in view of Ishiwatari *et al.* and, optionally, both of these further in view of Shi, *et al.*

The Examiner has further rejected claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 78, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146 and 148 under 35 U.S.C. §103(a) as being unpatentable over Rodriguez (US 5,889,189) in view of Gautier; et, al. and optionally, both of these further in view of Shi, *et al*.

The Examiner has further rejected claims 36-37, 43, 79-81 and 86 under 35 U.S.C. § 103(a) as being unpatentable over Rodriguez (U.S. 5,889,189) in view of Ishiwatari, *et al.* and optionally both of these further in view of Shi, *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38. 39, 40, 41,

42, 77, 78, 82, 83, 84, 85, 112, 113, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 133, 134, 136, 138, 140, 142, 144, 146, and 148 above, and further in view of Cho, *et al.* (In Vitro Cellular and Developmental Biology 34(3) part 2 (March 1998) p. 48A) or as being unpatentable over Rodriguez (US 5,889,189) in view of Gautier *et al.* (1998), European Journal of Biochemistry, 252:314-324), and optionally, both of these further in view of Shi, *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 78, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 above and further in view of Cho *et al.* (In vitro Cellular And Developmental Biology 34(3) part 2 (March 1998) p. 48A).

B. The Claimed Invention

Claims 35 and 78 have been canceled. Applicant has amended claims 32 and 77 to include the limitations of cancelled claims 35 and 78, respectively. Claim 32 is directed to "a transgenic monocot plant wherein at least a part of the plant comprises a recombinant nucleic acid comprising a promoter active in the part operably linked to a nucleic acid encoding a barley, rice *Arabidopsis*, soybean, wheat, tobacco or Brassica thioredoxin polypeptide wherein the promoter is *a seed or grain maturation-specific promoter*" (Emphasis added).

Claim 36 limits the transgenic plant of claim 32 to a promoter selected from the group consisting of rice glutenins, rice oryzins, rice prolamines, barley hordeins, wheat gliadins, wheat glutelins, maize zeins, maize glutelins, oat glutelins, sorghum kafirins, millet pennisetins, rye secalins, and maize embryo-specific globulin promoters.

Claim 37 further limits claim 32 to B1 and D hordein promoters.

Claim 43 further limits claim 42 to B1 and D hordein signal peptides.

Claim 77 is directed to "a transgenic monocot seed or grain comprising a recombinant nucleic acid comprising a promoter active in said seed or grain operably

linked to a nucleic acid molecule encoding a barley, rice *Arabidopsis*, soybean, wheat, tobacco, or Brassica thioredoxin polypeptide wherein said promoter is a *seed or grain maturation-specific promoter*" (Emphasis added).

Claim 80 further limits claim 77 to B1 and D hordein promoters.

Claim 81 further limits claim 77 to various seeds and grains.

Claim 86 further limits claim 85 to B-1 and D-hordein signal peptides.

C. The Prior Art

Rodriguez is directed to production of heterologous proteins by malting monocot plants. The heterologous genes are expressed during germination. (See Abstract). The Examiner admits that "[n]one of the previously cited references teach the use of a barley B1 Hordein promoter or signal peptide." The Examiner further states that "Rodriquez does specifically teach ... that the preferred transcription regulatory or provider region is chosen so as to be relatively silent except during seed *germination*" (Col 13 lines 42-44)." (Emphasis added.)

Ishiwatari *et al.* teach cDNA encoding a thioredoxin polypeptide from the monocot rice (Fig. 3), and that the polypeptide was overexpressed in *E. coli*. Ishiwatari *et al.* lack any disclosure or suggestion of a seed or grain maturation specific promoter.

Gautier *et al.* teach cDNA encoding a thioredoxin polypeptide from wheat, and overexpression in E. coli. Gautier *et al.* lack any disclosure or suggestion of a seed or grain maturation specific promoter.

Shi *et al.* teach isolation of thioredoxin cDNAs from soybean, and transformation of tobacco plants to study thioredoxin activity. Shi *et al.* lack any disclosure or suggestion of a seed or grain maturation specific promoter.

Cho et al. teach investigation of B-1hordein regulatory regions and subcellular localization signals in barley. Cho, et al. teach targeting of GUS protein and not thioredoxin. The reference became publicly available on April 22, 1998, and is Applicant's own publication. As such, Cho, et al. is not a proper prior art reference as deatiled below in the following argument, attached dated article, and attached declaration.

D. The Prior Art Distinguished

35 U.S.C. § 103(a) requires that "...differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). The *prima facie* case must satisfy three requirements: 1) the references must teach or suggest all the claim limitations; 2) the prior art combined with general knowledge must include a suggestion or incentive to modify or combine the references; and 3) the modification or combination must have a reasonable chance of success.

A. Rodriguez (US 5,889,189) in view of Ishiwatari et al. and, optionally, both of these further in view of Shi, et al.

The Examiner fails to satisfy the requirements to establish a *prima facie* case on multiple grounds. Specifically, 1) none of the cited references teach or suggest all the claim limitations; 2) the prior art combined with general knowledge fails to include a suggestion or incentive to modify the references; and 3) the references fail to teach that the modification would reasonable chance of success. Instead, the cited prior art teaches away from the claimed invention.

First, the references fail to teach all limitations of the claimed invention. Specifically, the claims, as amended, require a "seed or grain maturation-specific promoter." As defined in the specification at page 10, lines 22-25, a "maturation specific" promoter "has enhanced activity developmentally during the maturation of a part of the plant as compared to other parts of the plant and does not require its activity to

be limited to the development part of the plant." None of the cited references teach or suggest this limitation.

Rodriguez, the primary reference, teaches only the use of seed germination specific promoters. As the Examiner points out, the promoters of Rodriguez are "chosen to be relatively silent except during seed germination" Col 13, lines 44-45 (emphasis added). It is well known that seed germination is the process by which a mature seed germinates and begins to form a seedling. In contrast, seed maturation is the process by which a seed matures on a plant and this is not mentioned in Rodriguez. In addition, the secondary references fail to remedy the deficiencies of Rodriguez. Ishiwatara, *et al.* describe cDNA encoding a thioredoxin polypeptide from the monocot rice, but lack disclosure of a maturation-specific promoter. Shi, *et al.* describe a soybean thioredoxin, but also fail to describe a seed or grain maturation-specific promoter. The references thus fail to teach all claim limitations to the claimed invention.

Second, the references, separately or in combination, fail to provide the requisite motivation to combine their teachings to make the claimed invention. Rodriguez, the primary reference, actually teaches away from the claimed invention. The pending claims are limited to "a seed or grain maturation-specific promoter." Rodriguez, by contrast, guides one of ordinary skill in the art to use *seed germination specific promoters*. As the Examiner points out, the promoters of Rodriguez are "chosen to be relatively silent except during seed germination" Col 13, lines 44-45. One of ordinary skill in the art would thus be led away from incorporating maturation-specific promoters which function during seed maturation in the present invention.

Neither of the secondary references suggest or hint at a motivation to combine their teachings incorporating "maturation-specific promoters" as the limitation is defined in the Specification. Specifically, Ishiwatara *et al.* describe cDNA encoding a thioredoxin polypeptide from the monocot rice, but lack disclosure of a maturation-specific promotor. Shi, *et al.* describe a soybean thioredoxin but fail to describe a seed

or grain maturation-specific promoter. Accordingly, one of ordinary skill in the art would not be led to combine the references.

Third, the prior art provides no suggestion or reasonable expectation of success to combine their teachings. Rodriguez, as the primary reference, relates to the "production of heterologous proteins by malting of monocot plant seeds." See Abstract. As discussed above, Rodriguez's promoters are "chosen to be relatively silent except during seed germination," and are silent during seed maturation. Rodriguez thus teaches away from maturation-specific promoters. Ishiwatara *et al.* and Shi *et al.* both fail to suggest use of a maturation-specific promoter. Accordingly, one of ordinary skill in the art would have no reasonable expectation of success making a transgentic monocot plant comprising a maturation-specific promoter.

In view of the amendment and foregoing arguments, the prior art fails to render the claimed invention obvious.

B. Rodriguez (US 5,889,189) in view of Gautier; et, al. and optionally, both of these further in view of Shi, et al.

As in the previous rejection, the Examiner fails to satisfy the requirements to establish a *prima facie* case on multiple grounds.

First, the references fail to teach all limitations of the claimed invention. As discussed above and reiterated here, one of the cited references teach or suggest a "seed or grain maturation-specific promoter." Rodriguez, as discussed previously, teaches only the use of seed germination specific promoters. Gautier et al. describe a wheat thioredoxin, but fail to teach a seed or grain maturation-specific promoter. Shi et al., as discussed previously, describe a soybean thioredoxin, but also fail to teach or suggest a seed or grain maturation-specific promoter. The references in combination therefore fail to teach all limitations of the claimed invention.

Second, the references teach away from the claimed invention instead of providing the requisite motivation to combine their teachings to make the claimed invention. As discussed previously and reiterated here, Rodriguez teaches use of *seed germination specific promoters*. As the Examiner points out, the promoters of Rodriguez are "chosen to be relatively silent except during seed germination" Col 13, lines 44-45. Gautier *et al.* fails to suggest a maturation specific promoter. Shi, *et al.* describe a soybean thioredoxin, but also fail to describe a seed or grain maturation-specific promoter. Accordingly, one of ordinary skill in the art would be led to combine the references incorporating a germination specific promoter, not a maturation specific promoter.

Third, the prior art provides no suggestion or reasonable expectation of success to combine their teachings. As discussed previously and reiterated here, Rodriguez relates to the "production of heterologous proteins by malting of monocot plant seeds," and selects promoters that are "chosen to be relatively silent except during seed germination," and silent during seed maturation. Rodriguez thus teaches away from maturation-specific promoters. Gautier *et al.* and Shi *et al.* both fail to suggest use of a maturation-specific promoter. Accordingly, one of ordinary skill in the art would have no reasonable expectation of success making a transgentic monocot plant comprising a maturation-specific promoter since the prior art references as a whole teach away from the claimed invention.

In view of the amendment and foregoing arguments, the prior art fails to render the claimed invention obvious.

C. Rodriguez (U.S. 5,889,189) in view of Ishiwatari et al. and optionally both of these further in view of Shi, et al. (Plant Molecular Biology, 1996, 32:653-662), and further in view of Cho, et al.; OR Rodriguez (US 5,889,189) in view of Gautier et al., optionally, in further in view of Shi, et al., and further in view of Cho et al.

As in the previous rejections, the Examiner fails to satisfy the requirements to establish a *prima facie* case on multiple grounds. First, as discussed above, Rodriguez, Ishiwatari et. al., Shi et al., and Gautier et al. all fail to teach a "seed or grain maturation-specific promoter." Second, the cited prior art references not only fail to provide one of ordinary skill in the art with the requisite motivation to combine the prior art references, but teach away from the claimed invention. Third, one of ordinary skill in the art would

Cho et al. fail to cure the deficiencies of Rodriguez, Ishiwatari et. al., Shi et al., and Gautier et al., since the reference is unavailable as prior art.

not have a reasonable expectation of success in making the claimed invention, since the

prior art directs one of ordinary skill in the art toward germination specific promoters.

First, Cho, et al. was publicly available less than a year before the priority date of the instant application. The Examiner asserts that Cho et al. was published in March, 1998. However, "a journal article or other publication becomes available as prior art on [the] date it is received by a member of the public." MPEP §2128.02. As demonstrated by the attached, stamped reference, the publication by Cho et al. was received by the Lane Medical Library at Stanford University on April 22, 1998. The present application claims priority to provisional application 60/127,198, filed March 29, 1999. Accordingly, the publication was not publicly available more than one year prior to the priority date of the present application. The Examiner has not shown that the reference was available to the general public over a year prior to the present invention.

Second, Cho, et al. cannot be used as prior art under 35 U.S.C. §103, since the reference does not meet the statutory requirements of 35 U.S.C. 102(a). Section 35 U.S.C. 102(a) requires that the prior art be work of another. Several of the inventors of the present application are co-authors of the cited prior art reference. The inventors of the instant application are Myeong-Je Cho, Peggy G. Lemaux, Bob B. Buchanan, Joshua Wong, and Corina Marx. The authors of the Cho et al. reference are Myeong-Je Cho, C.D. HA, Bob B. Buchanan, and Peggy G. Lemaux. Applicants submit the attached Declaration under 37 CFR 1.131, stating that Applicants are the sole inventors, and that

C.D. HA, a non-inventor author of the Cho, et al. article, was merely working under the direction of the co-inventors. *See* MPEP §715.01(c). The Declaration further asserts that Joshua Wong and Corina Marx mutually conceived along with the other co-inventors and reduced to practice the invention based in part on the publication.

Therefore, since the Cho, et al. reference cited by the Examiner was 1) publicly available less than a year prior to the priority date of the present application and 2) was authored by the Applicants and is not of another, the reference does not constitute prior art.

The prior art therefore fails to render the pending claims obvious. In view of the claim amendments and arguments set forth above, Applicants respectfully request that rejections under 35 U.S.C. § 103 be withdrawn.

DOUBLE PATENTING REJECTIONS

The Examiner has provisionally rejected claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 78, 82, 83, 84, 85, 112, 114, 115, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 135, 136, 138, 140, 142, 144, 146, and 148 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8, 9, 10, 12, 15, 16, 17, 18, 63, 64, 72, 74, 75 and 76 of copending application number 09/540,014 filed March 31, 2000, in view of Rodriguez.

The Examiner has rejected claims 36-37, 43, 79-81 and 86 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8, 9, 10, 12, 15, 16, 17, 18, 63, 64, 72, 74, 75, 76 of copending application 09/540,014 in view of Rodriguez as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 78, 82, 83, 84, 85, 112, 114, 115, 116, 188, 120, 122, 124, 126, 128, 130, 132, 134, 135, 136, 138, 140, 142, 144, 146 and 148, above and further in view of Cho, *et al.*

Applicants submit the enclosed terminal disclaimer of 09/540,014 to obviate the double patenting rejection. In light of this submission, applicants request that the double patenting rejection be withdrawn.

37 CFR 1.78(c) and 35 U.S.C. §132 Showing

In response to the Examiner's request, applicants submit that application number 09/540,014 and the present application were subject to an obligation to assign to the University of California at the time both inventions were made. As such, the inventions of 09/540,014 and the present application were commonly owned at the time the invention in this application was made.

Related Application

Applicants identify commonly assigned related application 09/164,210. 09/164,210 and the present application were commonly owned at the time the invention in the present application was made.

Conclusions

In light of the above, Applicants submit that the pending claims are in condition for allowance. Should there be any remaining issues that remain unresolved, the Examiner is encouraged to contact the undersigned by telephone.

Attached hereto is a marked up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "<u>Version with</u> <u>Markings to Show Changes Made.</u>" A deleted item is indicated by brackets around the item, e.g., [and], while an insertion is <u>underlined</u>.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required,

applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing 416272001300. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: May 23, 2002

Respectfully submitted,

Michael P. Ware

Registration No. 38,651 Morrison & Foerster LLP

425 Market Street

San Francisco, California 94105-

2482

Telephone: (415) 268-6237 Facsimile: (415) 268-7522

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

At page 8, replace the paragraph starting at line 12 with the following new paragraph:

Thioredoxin protein or Thioredoxin polypeptide: A large number of plant, animal, and microbial thioredoxin proteins or polypeptides have been characterized, and the genes encoding many of these proteins have been cloned and sequenced. The present invention is preferably directed to the use of thioredoxin h proteins, although other thioredoxin proteins may also be employed to produce transgenic plants as described herein. Among the thioredoxin h proteins from plants that have been described to date are thioredoxin h proteins from Arabidopsis thaliana (Rivera-Madrid et al., 1993; Rivera-Madrid et at, 1995), Nicotiana tabacum (Marty and Meyer, 1991; Brugidou et al, 1993), Oryza sativa (Ishiwatari et al, 1995), Brassica napus (Bower et al., 1996), Glycine max (Shi and Bhattacharyya, 1996), and Triticum aestivum (Gautier et al., 1998). The amino acid sequences of these and other thioredoxin h proteins, and the nucleotide sequence of cDNAs and/or genes that encode these proteins, are available in the scientific literature and publicly accessible sequence databases. For example, a cDNA encoding thioredoxin h from Picea mariana is described in accession number AF051206 (NID g2982246) of GenBank, and located by a search using the Entrez browser/ nucleotide sequence search of the National Center for Biotechnology Information website, www.ncbi.nim.nih.gov]. The cDNA encoding the *Triticum aestivum* thioredoxin h protein used in the Examples described below is described on the same database under accession number X69915 (NID g2995377).

At page 14, replace the paragraph starting at line 26 with the following new paragraph:

IN THE CLAIMS

- 32. (Amended) A transgenic monocot plant wherein at least a part of said plant comprises a recombinant nucleic acid comprising a promoter active in said part operably linked to a nucleic acid encoding a [monocot]thioredoxin polypeptide wherein said promoter is a seed or grain maturation-specific promoter and said thioredoxin polypeptide is selected from the group consisting of barley, rice, *Arabidopsis*, soybean, wheat tobacco and Brassica thioredoxins.
- 36. (Thrice Amended) The transgenic plant of claim [35] <u>32</u> wherein said promoter selected from the group consisting of rice [glutelins] <u>glutenins</u>, rice oryzins, rice prolamines, barley hordeins, wheat gliadins, wheat glutelins, maize zeins, maize glutelins, oat glutelins, sorghum kafirins, millet pennisetins, rye secalins, and maize embryo-specific globulin promoters.
- 37. (Amended) The transgenic plant of claim 36 wherein said barley hordein promoter is selected [for] <u>from</u> the group consisting of B₋1 hordein and D₋hordein promoters.

- 38. (Amended) The transgenic plant of claim 32 wherein said monocot plant is selected from the group consisting of rice, barley, maize, wheat, oat, rye, sorghum, millet, triticale, [turf grass] turf grass and forage grass.
- 43. (Amended) The transgenic plant of claim 42 wherein said signal peptide is selected [for] from the group consisting of B_1 hordein and D_hordein signal peptides.

- 77. (Amended) A transgenic monocot seed or grain comprising a recombinant nucleic acid comprising a promoter active in said seed or grain operably linked to a nucleic acid molecule encoding a <u>barley, rice, Arabidopsis</u>, soybean, wheat, tobacco, or <u>Brassica</u> thioredoxin polypeptide <u>wherein said promoter is a seed or grain maturation-specific promoter.</u>
- 79. (Thrice Amended) The transgenic seed or grain of claim 77 [78] wherein said promoter is selected from the group consisting of rice glutelins, rice oryzins, rice prolamines, barley hordeins, wheat gliadins, wheat [glutelins] glutenins, maize zeins, maize glutelins, oat glutelins, sorghum kafirins, millet pennisetins, rye secalins, and maize embryo-specific globulin promoters.
- 80. (Amended) The transgenic seed or grain of claim [79] 77 wherein said barley hordein promoter is selected from the group consisting of B₋1 hordein and D₋ hordein promoters.
- 81. (Amended) The transgenic seed or grain of claim [80] <u>77</u> wherein said seed or grain is selected from the group consisting of rice, barley, maize, wheat, oat, rye, sorghum, millet, and triticale seed or grain.
- 82. (Amended) The transgenic seed or grain of claim 77 wherein said [monocot] thioredoxin polypeptide is thioredoxin h.
- 115. (Amended) The transgenic plant of claim 114 wherein said thioredoxin is barley thioredoxin $\underline{\mathbf{h}}$.

- 119. (Amended) The transgenic plant of claim 118 wherein said thioredoxin is wheat thioredoxin \underline{h} .
- 130. (Amended) The transgenic plant of claim 38 wherein said plant is forage or [turf grass] <u>turfgrass</u>.
- 133. (Amended) The transgenic seed or grain of claim 132 wherein said thioredoxin is rice thioredoxin \underline{h} .
- 135. (Amended) The transgenic seed or grain of claim 134 wherein said thioredoxin is barley thioredoxin \underline{h} .
- 139. (Amended) The transgenic seed or grain of claim 138 wherein said thioredoxin is wheat thioredoxin \underline{h} .